PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	Docket No: **Q101074**
Tomomichi Watanabe et al	Conf. No.: **9679**
Appln. No.: **10/547,843**	Group Art Unit: **1649**
Filed: **September 6, 2005**	Examiner: **Chernyshev, O.**

For: **NOVEL PROTEIN AND ITS DNA**

DECLARATION UNDER 37 C.F.R. § 1.132

MAIL STOP AMENDMENT
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, Tomomichi Watanabe, hereby declare and state:

THAT I am a citizen of JAPAN, residing at 9-12,Takehashi-cho, Ibaraki-shi, Osaka, Japan;

THAT I have received the degree of Master of Biology in March, 2000 from Osaka University;

THAT I have been employed by Takeda Pharmaceutical Company, Ltd., Osaka, Japan since April, 2000, engaged in research of Alzheimer's disease in the Pharmaceutical Research Division of said company;

THAT I have been appointed an Assistant Research Head of Pharmaceutical Research Division of Takeda Pharmaceutical Company, Ltd.;

THAT I have published, with other research workers, a number of reports on scientific studies, among others, including

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1. The carboxy terminus of the small subunit of TFIIE regulates the transition from transcription initiation to elongation by RNA polymerase II; Mol.Cell.Biol., 23, 2914 (2003);

2. Studies of Schizosaccharomyces pombe TFIIE indicate conformational and functional changes in RNA polymerase II at transcription initiation; Genes.Cells., 10, 207 (2005);

3. Modulation of TFIIH-associated kinase activity by complex formation and its relationship with CTD phosphorylation of RNA polymerase II; Genes.Cells., 5, 407 (2000)

In order to demonstrate that the data shown in Example 4 of the patent application No. 10/547,843 is statistically significant, I conducted the following experimentation.

Under the same experimental conditions as those in Example 4 of the patent application No. 10/547,843, assays were conducted for the cell death promotion activity of C1 five times using CELL DEATH DETECTION ELISA ^{PLUS} kit (Roche). The results are shown in Figure 1 and Figure 2 below. The relative amount of cleaved DNA (in terms of OD405-492 readings) in a cell after 24 hours and 48 hours of stimulation with tunicamycin in comparison to control without tunicamycin stimulation is shown in Figure 1 and Figure 2, respectively.

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Figure 1

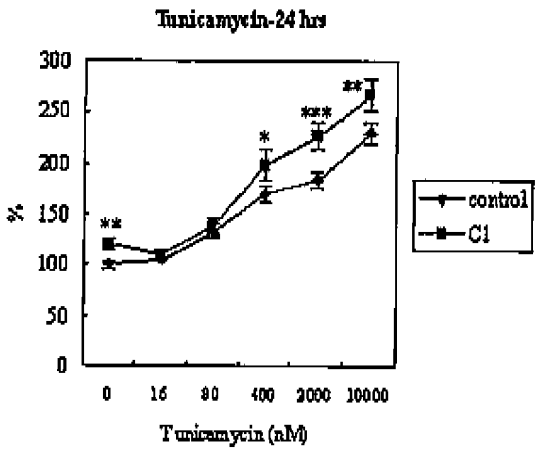
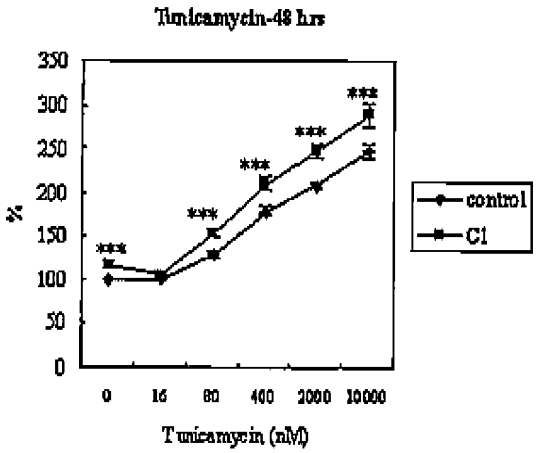


Figure 2



As a result of having held t-tests for the C1-introduced cells and the control for the concentrations of tunicamycin indicated by asterisks, the C1-introduced cells significantly promoted the tunicamycin-stimulated cell death in comparison to the control (P*<0.05, P**<0.01, P***<0.001).

Furthermore, I conducted assays for evaluating cell death promotion activity of DP5 gene, which is known to induce cell death (J. Biol. Chem. 1999:274 p7975-), under the same experimental conditions as those in Example 4 of the patent application No. 10/547,843. The results are shown in Figures 3 to 6 below. The amount of cleaved DNA (in terms of OD405-492) in a cell after 24 hours and 48 hours of stimulation with tunicamycin or thapsigargin in comparison to the control is shown. As shown, DP5 showed cell death promotion activity of

almost the same level as that observed for C1 in Example 4 of the patent application No. 10/547,843.

Figure 3

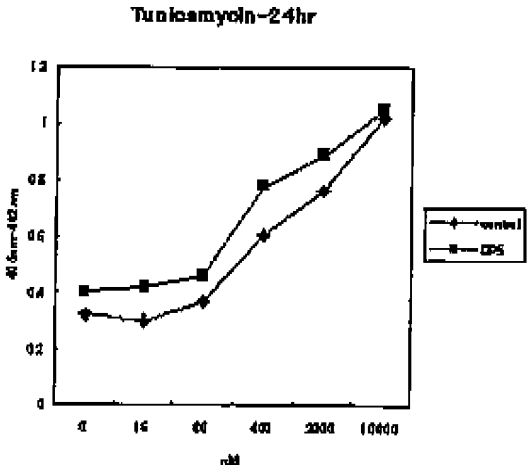


Figure 4

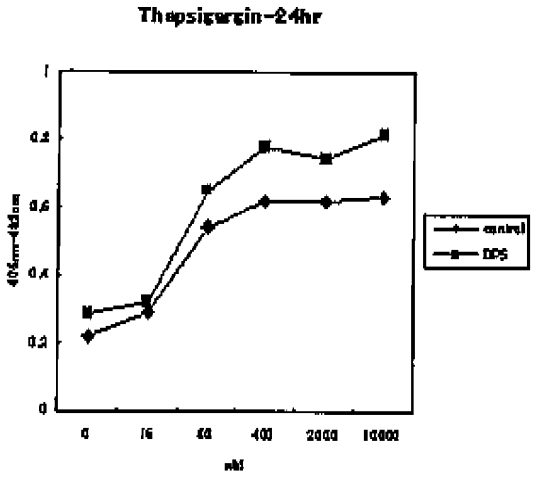


Figure 5

Figure 6

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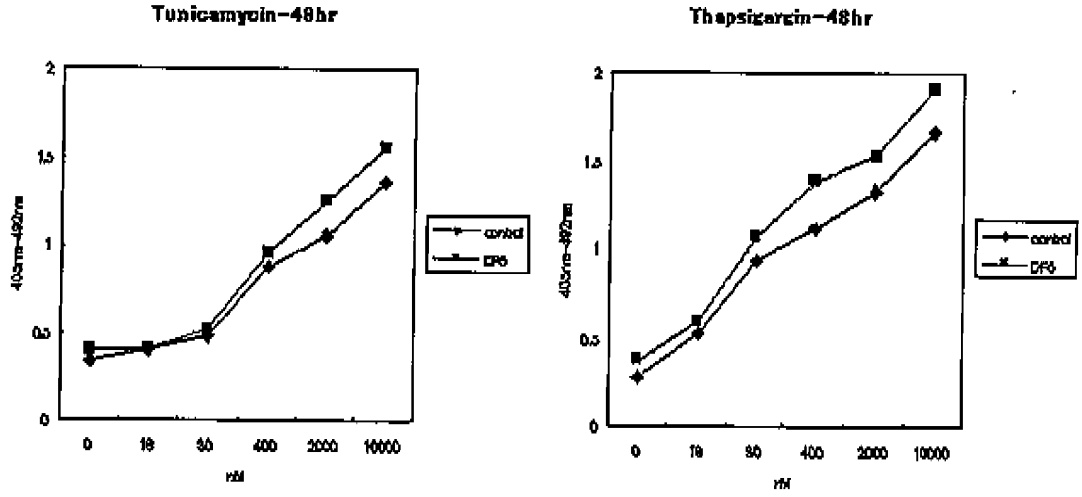


Since it was known to a person of ordinary skill as of the priority date of the patent application No. 10/547,843 that DP5 had cell death promotion activity, it should be concluded that C1, also exhibits cell death promotion activity similar to that of DP5 based on the results shown in the Figures above. For at least these reasons, it should be concluded that the cell death promotion activity of C1 shown in Example 4 of the patent application No. 10/547,843 is statistically significant.

With regard to the statistical significance of the data shown in Example 5 of the patent application No. 10/547,843, I provide the following comments.

In an experiment of gene transfer such as that in Example 5, it is common practice that a vector having been used for transduction of the gene of interest, a LacZ vector, or a GFP expression vector is used for verification of the experiment as a control in order to exclude any

effect from the employed gene transduction process. In the experiment shown in Example 5, no data is shown for comparison between the cell used for the gene transfer and the wild-type cell, which is in conformity to the common practice explained above.

Nevertheless, I conducted experiments to show that there was no observed difference in the Aβ secretion between wild-type cells, in which a vector with no gene for expression is introduced, and cells transformed with a GFP expression vector (control cells shown in Example 5) (see Figure 7 and 8 below).

Figure 7

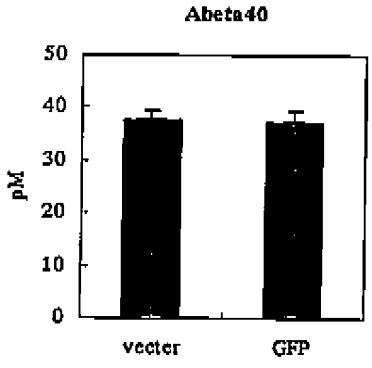
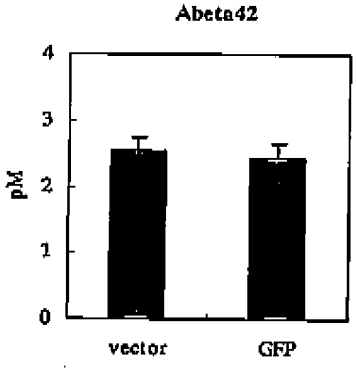


Figure 8



Thus, in view of the knowledge of a person of ordinary skill as of the priority date of the patent application of 10/547,843, and from the results shown in Example 5, in which an inhibitory activity of C1 against Aβ secretion as compared to GFP as a control is presented, it should be concluded that C1 has the inhibitory activity against the Aβ secretion.

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I declare further that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Date: March 3, 2008

Tomomichi Watanabe
Tomomichi Watanabe